REMARKS/ARGUMENTS

The Pending Claims

Claims 35, 39-42, 45-48, and 50-53 are pending and are directed to a method of changing the sensory perception of an animal.

The Amendments to the Claims

Claim 35 has been amended to incorporate the subject matter of claims 38 and 49, and to delete part (b). Claims 36-38, 43, 44 and 49 have been cancelled. Claims 50 and 51 have been amended to reflect the cancellation of claim 49. Accordingly, no new matter has been added by way of these amendments.

The Office Action

Claims 35-53 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Claims 35-53 are rejected under 35 U.S.C. § 112, first paragraph, for allegedly introducing new matter into the disclosure of the present application. Claims 35-53 also are rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. Claims 35-53 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent No. 6,838,444 (Zoghbi et al. - "the Zoghbi patent") and Roy et al., *J. Virol.*, *72*(8): 6875-6879 (1998) ("the Roy reference") alone, or in further view of U.S. Patent 6,821,775 (Kovesdi et al. - "the Kovesdi patent"), Staecker et al., *Otolaryngol. Head Neck Surg.*, *119*(1): 7-13 (1998) ("the Staecker reference"), and/or U.S. Patent 6,455,314 (Wickham et al. - "the Wickham patent"). Reconsideration of these rejections is respectfully requested.

Discussion of Rejection Under 35 U.S.C. § 112, Second Paragraph

The Office Action alleges that claims 35-53 are indefinite under Section 112, second paragraph, for the following reasons: (a) the specification allegedly does not define the phrase "a promoter that specifically functions in supporting cells of the inner ear," (b) it is allegedly unclear whether the phrase "comprising a non-native ligand, which non-native ligand enhances uptake of the adenoviral vector" recited in claim 35 modifies the recited chimeric coat protein, adenoviral vector, or pharmaceutical composition, (c) the phrase "a chimeric coat protein ablated for binding to a native adenovirus receptor" recited in claim 35

is unclear in the context of a non-group C adenoviral vector, and (d) the term "non-group C adenoviral vector" is unclear.

Contrary to the assertion of the Office Action, one of ordinary skill in the art would understand the meaning of the phrase "a promoter that specifically functions in supporting cells of the inner ear" based on the disclosure of the present application. In this regard, the specification defines a "tissue-specific" promoter as "a promoter that is preferentially activated in a given tissue and results in expression of a gene product in the tissue where activated" (see specification at, e.g., paragraph 0055). Such promoters are disclosed in the application (e.g., a hes-1 promoter), and were known in the art at the time the present application was filed (see, e.g., Rio et al., *J. Comp., Neurol.*, *442*: 156-162 (2002), Forge and Wright, *British Medical Bull.*, *63*: 5-24 (2002), Zajic et al., *Hear. Res.*, *52*(1): 59-71 (1991), Takumi et al., *Eur. J. Neurosci.*, *10*(12): 3584-95 (1998), Lewis et al., *Mech. Dev.*, *78*(1-2): 159-63 (1998), Lautermann et al., *Cell Tissue Res.*, *294*(3): 415-20 (1998), Heller et al., *Proc. Natl. Acad. Sci. USA*, *95*(19): 11400-5 (1998), Kwun et al., *Hear. Res.*, *183*(1-2): 84-96 (2003), and Holt et al., *J. Neurophysiol.*, *81*(4): 1881-8 (1999)).

The Office Action further alleges that the phrases "comprising a non-native ligand..." and "a chimeric coat protein..." render claim 35 indefinite. Claim 35 has been amended to delete these phrases, thereby rendering these aspects of the rejection moot.

The Office Action alleges that it is unclear as to whether the term "non-group C adenoviral vector" includes a group C adenoviral vector comprising sequences derived from another adenovirus serotype (e.g., a serotype 5 adenovirus comprising a chimeric Ad5-Ad12 hexon protein). While Applicants disagree with these aspects of the rejection, claim 35 has been amended to recite that the pharmaceutical composition comprises a subgroup A, B, D, E, or F adenoviral vector.

In view of the foregoing, one of ordinary skill in the art would understand the metes and bounds of claim 35, as well as the claims depending therefrom. Accordingly, the rejection under Section 112, second paragraph, should be withdrawn.

Discussion of Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 35-53 are rejected under Section 112, first paragraph, as allegedly introducing new matter and lacking enablement. These rejections are traversed for the reasons set forth below.

A. New Matter

According to the Office Action, the specification does not disclose a chimeric coat protein in the context of a non-group C adenoviral vector, or the native adenovirus receptor of a non-group C adenoviral vector. Applicants note that claim 35, as amended, no longer recites a chimeric coat protein ablated for binding to a native adenovirus receptor. As such, this aspect of the new matter rejection is rendered moot by the amendments to claim 35.

The Office Action further alleges that the specification does not define the phrase "a promoter that specifically functions in the inner ear" and does not disclose any examples of such promoters. While the Office Action concedes that the application discloses that the hes-1 promoter specifically functions in supporting cells, the Office Action alleges that the application does not disclose that the activity of the hes-1 promoter is exclusive to supporting cells of the inner ear. As discussed above, the specification defines a "tissue-specific" promoter as "a promoter that is preferentially activated in a given tissue and results in expression of a gene product in the tissue where activated" (see specification at, e.g., paragraph 0055). In addition, it was known in the art at the time the present application was filed that the Hes1 gene is expressed in supporting cells of the inner ear and not in other cell types of the inner ear (see, e.g., Zheng et al., *Development*, *127*: 4551-4560 (2000)). Other genes that are expressed specifically in supporting cells of the mammalian inner ear also were known in the art at the time the present application was filed (see, e.g., Rio et al., *J. Comp., Neurol.*, *442*: 156-162 (2002), Forge and Wright, *British Medical Bull.*, *63*: 5-24 (2002), Zajic et al., *Hear. Res.*, *52*(1): 59-71 (1991), Takumi et al., *Eur. J. Neurosci.*, *10*(12): 3584-95 (1998), Lewis et al., *Mech. Dev.*, *78*(1-2): 159-63 (1998), Lautermann et al., *Cell Tissue Res.*, *294*(3): 415-20 (1998), Heller et al., *Proc. Natl. Acad. Sci. USA*, *95*(19): 11400-5 (1998), Kwun et al., *Hear. Res.*, *183*(1-2): 84-96 (2003), and Holt et al., *J. Neurophysiol.*, *81*(4): 1881-8 (1999)).

For the foregoing reasons, the subject matter of the pending claims, as amended, is fully supported by the present application. Therefore, the subject matter of the pending claims does not introduce new matter into the present application, and the rejection under Section 112, first paragraph, should be withdrawn.

B. Enablement

The Office Action contends that the specification does not enable the claimed method when the adenoviral vector comprises a nucleic acid sequence encoding *any* atonal-associated factor (other than *Math1*, *Hath1*, and *Atoh1*) operably linked to a promoter that specifically functions in supporting cells of the inner ear.

While Applicants disagree with this rejection, claim 35 has been amended to recite an adenoviral vector comprising a nucleic acid sequence encoding *Hath1*. Thus, this aspect of the enablement rejection is rendered moot by the amendments to claim 35.

The Office Action contends that the specification fails to provide any guidance as to the identity and use of a promoter that functions specifically in supporting cells of the inner ear. As discussed above, the application discloses that the hes-1 promoter specifically functions in supporting cells of the inner ear (see, e.g., paragraph 0055), and the prior art demonstrates that the Hes1 gene is expressed in supporting cells of the inner ear and not in other cell types of the inner ear (see, e.g., Zheng et al., *supra*). Other genes that are expressed specifically in supporting cells of the mammalian inner ear also were known in the art at the time the present application was filed (see, e.g., Rio et al., *J. Comp., Neurol.*, *442*: 156-162 (2002), Forge and Wright, *British Medical Bull.*, *63*: 5-24 (2002), Zajic et al., *Hear. Res.*, *52*(1): 59-71 (1991), Takumi et al., *Eur. J. Neurosci.*, *10*(12): 3584-95 (1998), Lewis et al., *Mech. Dev.*, *78*(1-2): 159-63 (1998), Lautermann et al., *Cell Tissue Res.*, *294*(3): 415-20 (1998), Heller et al., *Proc. Natl. Acad. Sci. USA*, *95*(19): 11400-5 (1998), Kwun et al., *Hear. Res.*, *183*(1-2): 84-96 (2003), and Holt et al., *J. Neurophysiol.*, *81*(4): 1881-8 (1999)).

Accordingly, using the guidance provided by the specification in combination with the knowledge in the art at the time the present application was filed, one of ordinary skill in the art would be able to make and use the claimed invention without undue experimentation.

Thus, Applicants request withdrawal of the enablement rejection under Section 112, first paragraph.

Discussion of Rejections Under 35 U.S.C. § 103(a)

Claims 35-53 have been rejected under Section 103 as allegedly obvious over the Zoghbi patent and the Roy reference alone, or in further view of the Kovesdi patent, the Staecker reference, and/or the Wickham patent. These rejections are traversed for the reasons set forth below.

The Zoghbi patent discloses a method of generating hair cells in an animal (e.g., a human) comprising delivering to the inner ear of the animal a nucleic acid encoding an atonal-associated factor using, for example, an adenoviral vector. The Office Action acknowledges, however, that the Zoghbi patent does not disclose the use of a non-group C adenoviral vector comprising a nucleic acid sequence encoding an atonal-associated factor and a chimeric coat protein ablated for binding to a native adenovirus receptor and comprising a non-native ligand.

The Roy reference discloses a serotype 5 adenoviral vector that comprises hexon sequences from a serotype 12 adenovirus. The Office Action concludes that it would have been obvious to one of ordinary skill in the art to combine the method disclosed in the Zoghbi patent with the adenoviral vector disclosed in the Roy reference, and thereby arrive at the claimed invention.

The rejections under Section 103 appear to be based on the Office Action's interpretation of the term "non-group C adenovirus." Specifically, the Office Action considers an Ad5 vector comprising an Ad12 hexon protein to be a "non-group C" adenoviral vector.

Claim 35, as amended, recites a pharmaceutical composition comprising a subgroup A, B, D, E, or F adenoviral vector comprising a nucleic acid sequence encoding *Hath1* operably linked to a promoter that specifically functions in supporting cells of the inner ear. Neither the Zoghbi patent nor the Roy reference discloses or suggests a subgroup A, B, D, E, or F adenoviral vector encoding *Hath1*.

None of the secondary references cited by the Office Action compensates for the deficiencies of the Zoghbi patent and the Roy reference. The Kovesdi patent discloses an E1/E3/E4-deficient serotype 5 adenoviral vector encoding a pigment epithelium-derived factor (PEDF). The Staecker reference discloses a method of transfecting auditory hair cells with an HSV vector encoding brain-derived neurotrophic factor. The Wickham patent discloses recombinant adenovirus fiber proteins that are modified to reduce affinity for the CAR cellular receptor. None of the secondary references discloses or suggests a method of changing the sensory perception of an animal, which comprises administering to the inner ear a pharmaceutical composition comprising a subgroup A, B, D, E, or F adenoviral vector comprising a nucleic acid sequence encoding *Hath1* operably linked to a promoter that specifically functions in supporting cells of the inner ear.

Moreover, in view of the variation in genomic sequence conservation across different adenovirus groups, it would not have been obvious to generate a non-group C adenoviral vector based on a disclosure of generating a group C adenoviral vector. In this respect, at least 20-50% of the adenoviral genome is known to vary between groups (see, e.g., Horwitz, "Adenoviridae and Their Replication," in Fields et al. (eds.), *Fundamental Virology*, Raven Press Ltd., New York, NY (1991)).

In view of the foregoing, the subject matter of the pending claims is not obvious in view of the cited references, either alone or in combination. Accordingly, the rejections under Section 103 should be withdrawn.

Conclusion

Applicants respectfully submit that the patent application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned agent.

Respectfully submitted,

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